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wherein

R_1, R_3 independently represent NH_2, an amino acid or a peptide containing up to 100 amino acids; and

R_2, R_4 independently represent COOH, $CONH_2$ an amino acid or a peptide containing up to 100 amino acids;

and the amidated, acetylated, sulfated, phosphorylated, glycosylated, oxidized derivatives or fragments thereof having bifidogenic properties.

REMARKS

The instant Amendment enters on the record the substitute paper copy of the Sequence Listing, submitted at the same time, herewith.

Also, the specification and claims are amended, hereby, to include the corresponding SEQ ID numbers from the Sequence Listing (marked up pages of the specification are attached). Claim 5 replaces claim 2, in order to recite the SEQ ID numbers in the claim.

Favorable action is requested.

Respectfully submitted,

By William E. Player

William E. Player
Registration No. 31,409

Date: August 20, 2001
JACOBSON HOLMAN PLLC
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Telephone: (202) 638-6666
Atty. Docket No.: P65141US0
WEP/vjb
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Fraction 9 contained the pure bifidogenic component:

YQRRPAIAINNPYVPRTYYANPAVVRPHAQIPQRQYLPNSHPPTVVRRPNLHPSF

(casein K-63-117);

fraction 10 contained the bifidogenic component:

GRRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPICCIQA

(neutrophile lactoferrin-20-67);

and fraction 11 contains the bifidogenic component with an adduct mass of +16, which indicates that it is an oxidation product (probably, one methionine has been oxidized).

Both peptides and the oxidation product exhibit bifidogenic activity.

Example 2

Demonstration of the growth-regulating activity on E. coli

Fractions from the HPLC were employed with *E. coli* K12. The test is performed in 3 g/l tryptic soy broth (Sigma) as follows:

For each assay, cultures of *E. coli* K12 were freshly inoculated in tryptic soy broth (Sigma, Deisenhofen, Germany, order No. T8907) (Difco Manual, 10th ed., p. 1027). The incubation of these bacteria was always performed under aerobic conditions at 37 °C for 16 hours. Peptides to be tested were given to a test solution consisting of 200 µl of 3 g/l tryptic soy broth in 96-well cell culture plates, and inoculated with 20 µl of a diluted bacterial suspension. The photometric absorption of the inoculum was 0.05, meas-

infantile intestinal flora, and they promote the growth of desired bacteria, such as bifidobacteria, by promoting the growth of bifidobacteria more than that of other bacteria or by selectively inhibiting the undesired bacteria. This property of providing bifidobacteria with an advantage with respect to growth is called "bifidogenic".

Preferably, peptides are used which have the following amino acid sequence:

R_1-EQLLRLKK-R_2, R_1-YLEQLLRLKKY-R_2, R_1-NRQRNILR-R_2,
R_1-YMNGMNRQRNILR-R_2, R_1-FQWQRNMRK-R_2, R_1-HTGLRRTA-R_2,
R_1-FTAIQNLRK-R_2, R_1-EVAARARVVW-R_2, R_1-WQRNMRKV-R_2,
R_1-LARTLKRLK-R_2, R_1-YKQKVEKV-R_2, R_1-LVRYTKKV-R_2,
R_1-KYLYEIARR-R_2, R_1-ARRARVVWCAVG-R_2, R_1-ARRARVVWCAVGE-R_2,
R_3-CIAL-R_4 R_3-CIAL-R_4

R_1-YQRRPAIAINNPYVPRTYYANPAVVRPHAQIPQRQYLPNSHPPTVVRRPNLHPSF-R_2,
R_1-GRRRRSVQWCTVSQPEATKCFQWQRNMRRVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-GRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-GRRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-VYQHQKAMPKPWIQPKTKVIPYVRYL-R_2, R_1-ARRARVVWAAVG-R_2,
R_1-CAVGGGCIAL-R_2,
R_1-RHTRKYWCRQGARGGCITL-R_2.

wherein

R_1, R_3 independently represent NH_2, an amino acid or a peptide containing up to 100 amino acids; and

R_2, R_4 independently represent COOH, $CONH_2$, an amino acid or a peptide containing up to 100 amino acids;

and the amidated, acetylated, sulfated, phosphorylated, glycosylated, oxidized derivatives or fragments thereof having bifidogenic properties.

Fraction 9 contained the pure bifidogenic component: (SEQ ID NO: 17)

YQRRPAIAINNPYVPRTYYANPAVVRPHAQIPQRQYLPNSHPPTVVRRPNLHPSF

(casein K-63-117);

fraction 10 contained the bifidogenic component: (SEQ ID NO: 19)

GRRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPICCIQA

(neutrophile lactoferrin-20-67);

and fraction 11 contains the bifidogenic component with an adduct mass of +16, which indicates that it is an oxidation product (probably, one methionine has been oxidized).

Both peptides and the oxidation product exhibit bifidogenic activity.

Example 2

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infantile intestinal flora, and they promote the growth of desired bacteria, such as bifidobacteria, by promoting the growth of bifidobacteria more than that of other bacteria or by selectively inhibiting the undesired bacteria. This property of providing bifidobacteria with an advantage with respect to growth is called "bifidogenic".

Preferably, peptides are used which have the following amino acid sequence: (SEQ ID NO: 1-24, respectively in order of appearance)

R_1-EQLLRLKK-R_2, R_1-YLEQLLRLKKY-R_2, R_1-NRQRNILR-R_2,
R_1-YMNGMNRQRNILR-R_2, R_1-FQWQRNMRK-R_2, R_1-HTGLRRTA-R_2,
R_1-FTAIQNLRK-R_2, R_1-EVAARARVVW-R_2, R_1-WQRNMRKV-R_2,
R_1-LARTLKRLK-R_2, R_1-YKQKVEKV-R_2, R_1-LVRYTKKV-R_2,
R_1-KYLYEIARR-R_2, R_1-ARRARVVWCAVG-R_2, R_1-ARRARVVWCAVGE-R_2,
R_3-CIAL-R_4 R_3-CIAL-R_4

R_1-YQRRPAIAINNPYVPRTYYANPAVVRPHAQIPQRQYLPNSHPPTVVRRPNLHPSF-R_2,
R_1-GRRRRSVQWCTVSQPEATKCFQWQRNMRRVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-GRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-GRRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2,
R_1-VYQHQKAMPKPWIQPKTKVIPYVRYL-R_2, R_1-ARRARVVWAAVG-R_2,
R_1-CAVGGGCIAL-R_2,
R_1-RHTRKYWCRQGARGGCITL-R_2.

wherein

R_1, R_3 independently represent NH_2, an amino acid or a peptide containing up to 100 amino acids; and

R_2, R_4 independently represent COOH, $CONH_2$, an amino acid or a peptide containing up to 100 amino acids;

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